

A)

	Motif 1	Motif 2	Motif 3	Motif 4	
Rv2837c_Mt	VGVCVHVHPADDTIGAGLALALVLDGCG	[35] VDLVVTVDIPSVDRLGALG	[6] RELLVJDHFEASND	[10] SADSTTTWVAEILDMWGKPIDRVAHCIVAGLATD	TGSPRWASV
s111253_Ssp	DLILCHQTADPDVLAAGVGLAKLHPSGR	[34] IRSYVIVENQOQDRLGKAA	[8] RQVAIVDHFELNSP	[11] AVGASTTLIVEKLRADISLSMVEASVMALGIHVD	TGSLTFTQT
MGPA_Mg	IVIPHHVRPDGCLGAQOGLFHLIKANF	[32] EALAIVDQANVKNRIELRE	[7] KAVLRDHPHPNED	[11] SYVACCEQIVEMATVAKWTIPPVATALLVIGIYTD	SNRFLYSNT
YTOI_Bs	IILHRHVRPDPAYGSCQGLTEILRETY	[30] GALVIVDPTANQERIDQOR	[4] AKLMKDPHPNED	[13] SVSEMIYELYLEGKEHGWKLNKRAELIYAGIVGD	TGGRFLFPNT
AF2029_Af	LGIFTHDNPDPSMSSAYALREIAKQFD	[37] YDAFAIVDSGPGVNNISIP	[3] DISIVJDHPHPAEK	[10] DVGATATILTEYIKELKITPSKILATATLPFGIKS	ETDEPKRNR
MJ0977_Mj	NKILIVTHIDTGLTSRAILQKLABRLN	[23] YDLTIPADLGSGQLKMIKE	[11] DKIIIDHPHQPEE	[18] GAEICGAGVSYLFAKAINNDWIDLAKYAVLGA	VGDIQNIEGKLI
MJ1198_Mj	RPIIRHHPDGYCGGTALEKAILPII	[46] LPLVLIDNGSTDEDIPAI	[7] IEVIVJDHPHPGE	[85] KGRTYDREYLEKIALCWDFEAFYLRFMDGK	GIVDDILATNIEKF
HP1042_Hp	MQVYHLSHIDJGYACQLVSKQFFKNIQ	[27] EFLIVSDNLNLNEAEVL	[13] IQIQLDHPHISGK	[19] IVYEFLKXHYAILEPKNTTWLEPLVEMVNSVD	IMDTQGYGFELG
RecJ_Hi	QKIVIVGDFADGATSTALSVALRQLG	[31] VQLMTVDNGVSSFDGVAF	[5] IRVLVDHPHELPE	[33] LAVRAKFRLEGIFTAETQPNFTDLDLVALGTIAD	VVPLDQNNR
RecJ_Hp	TEILVVGDIYDADGVISSAIMAKFPESLN	[27] APLIITVDNGINAFEAARF	[5] YTLIIDHPHECLHH	[27] LVAFYLCYGIHQHLLGKEKSHSSSELLCLAGVATIA	DNMPLTFFNR
RecJ_Ssp	EKVINGDFPDGIGITSTAVLWEGLGQFF	[32] TKLIIVDPTGTNLDIYV	[5] MDVIVDHPHTLPD	[27] VAFKLVBALYNQYPTVPQPLEDLDLVAIGLIA	DLVLTQGDGR
YYBQ_Bs	ILIFGHQNPDTTICSAIYAYADLNKILG	[36] VNGVELVDHNERQQSIKDI	[3] QVLEVJDHERIAN	[12] PVGCTATILNKMYKENNVKIEKIEIAGLMLSA	IISSDLLFKSPIC
ICRA_Sg	ILVFGHQNPDSDAIGSSYAFAYLAREAY	[38] AEQVLTLDHNEFQQSVADI	[3] EVYGVJDHERVAN	[12] PVGSASSIVYRMFKHSHSVAVSKIEIAGLMLSG	LISDTLLKSPIT
Y608_Mj	RYVWGHKNPDTSIASAIYLAFLDCYP	[31] GKEHTLVDPHSEKSSQSFDDL	[3] KLIAIDHPHKVGL	[19] IAELYFKDAIDLIGGKKKELKPDLAGLLLSATIS	SDTVLFKSPIT
AF0756_Af	VTVVGHKNPDTSVCSAIAFAFAYLWKNWK	[46] GKVALVDPHSEKAQTVDGI	[3] EWVAIVDHPHKIGD	[12] PVGCTATVIKLLFDKTGVEIPKDIAGILLSSIL	SDTVIFKSATT
U60409_Lm	TWVQNEGDDDSIVGCIYLAFLPKQP	[44] QIAHNLVDIAALNASVLY	[14] RWGVJDHPHFDEQ	[11] LRTVGSACTLVTELYRECGEDVVCPTLLTAP	IVLDTVNFEPQAK
PPX1_Sc	TICVGNESADDSIASAITYSYCYIYN	[62] ELNSVLVDNDTPKNLKNY	[2] NVVGEJDHPHFDEQ	[14] SCSSLVFNWYVEKLQGDREVVMNIAPLLMGAIL	IDTSNMRRKVB
PRUNE_Dm	HLVMGNESQDLDSAVSATVLAFFVQAQRH	[48] DVNVTLVDHVSPLAPNVT	[1] NVTEIJDHPLEPD	[18] SVGSCATLVAQRYLAEDQPRSTSVQAQLLHAT	IVLDTINPAPAAK
h-prune.1_Hs	HVVVLGNEAOELDSTVSALALAFYLAKTT	[52] QLTLLVDHHLISKSDTAL	[2] AVEVLJDHPPIEP	[12] LVGSCATLVTERILQGAPEILDORTAALLHGT	IIIDCVNMDLKIG

	Specific motifs	G18	
Rv2837c_Mt	[107] TVNLAAVSGFGGGRHLRAGYTTTGS	1648883	/
s111253_Ssp	[123] DTDLTQLLEPYGCGGHAQAANLRDV	1653244	
MGPA_Mg	[102] GINVRDIAIKYGGGHNNAAGAIITNK	1045875	
YTOI_Bs	[103] GPVINGLARKYNGGGHPLASGASIYSW	2293259	
AF2029_Af	[102] EVLRRAFGDVGSAGGHAHAAGAQIPLG	2648507	
MJ0977_Mj	[254] AIKYASEKVGSGGGHKKFACGAYIPDN	2128614	
MJ1198_Mj	[109] QLMEBIPEASLDGGGHECAGSLKFVEG	2128720	
HP1042_Hp	[137] CDVCELSQWCFNGGGHNRNAGGKIDGF	2314198	
RecJ_Hi	[168] RIHSQHNMILKFGGHAMAAGLSIRBE	1172895	
RecJ_Hp	[155] DALNGVSSLLLYGGHRRQACGLSVEKN	2313437	
RecJ_Ssp	[165] ALLHSQHMLMGFGGHPFAAGLSLPLD	1652638	/
YYBQ_Bs	[31] DLSKKTVEELISLDAKEPTLG	[75] TALLKGVSRRKKQVWPVLTD	586817
ICRA_Sg	[31] NLAKSAEELIDIDAKTFELN	[75] HAPLAGAVSRKKQVWPQLTE	1743856
MJ0608_Mj	[32] VVGKLKPEEILNMDFKNFDFN	[74] SVFLEGVMSRKKQVWPPLER	1591318
AF0756_Af	[32] AVDDLTAMDIIKRDYKDFDMS	[75] SVWLDGVMRKKQVWPVPLEK	11498362
L2759.9_Lm	[36] DVLAISVPQILRRDYKQFSFK	[105] YSLSDPSISRKK-LVPALSE	1407725
PPX1_Sc	[41] DIKGFVSVDILKDYKQFNQ	[97] MFKQLNVEATRKQVWPVLEE	730369
PRUNE_Dm	[37] DISKLTLEVLKDKMKVLQTD	[97] LRQHNVAQTRKH-ILPIVKR	1079081
h-prune.1_Hs	[34] DVSGLTTEQMLRKDQKTIYRQ	[94] YLQGNTOQVSRKK-ILPLLQE	11245938

Family 2

Fig. 1

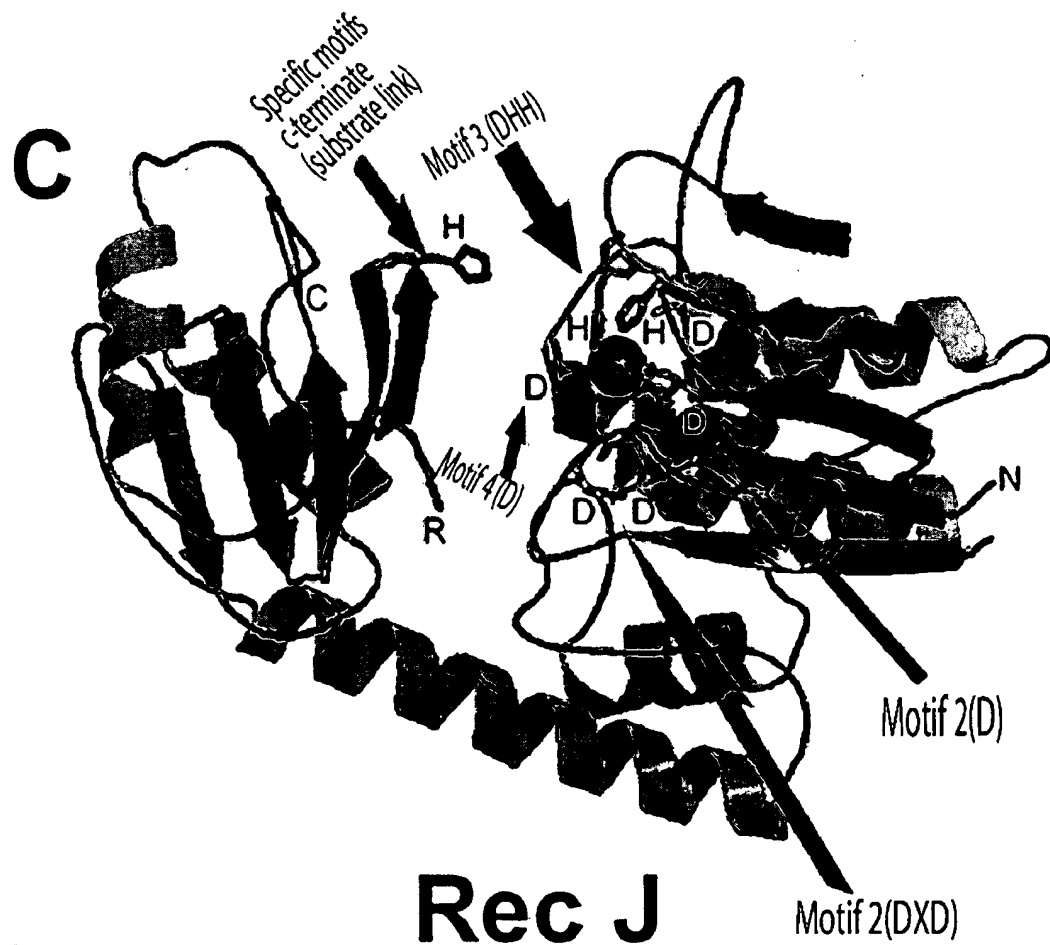
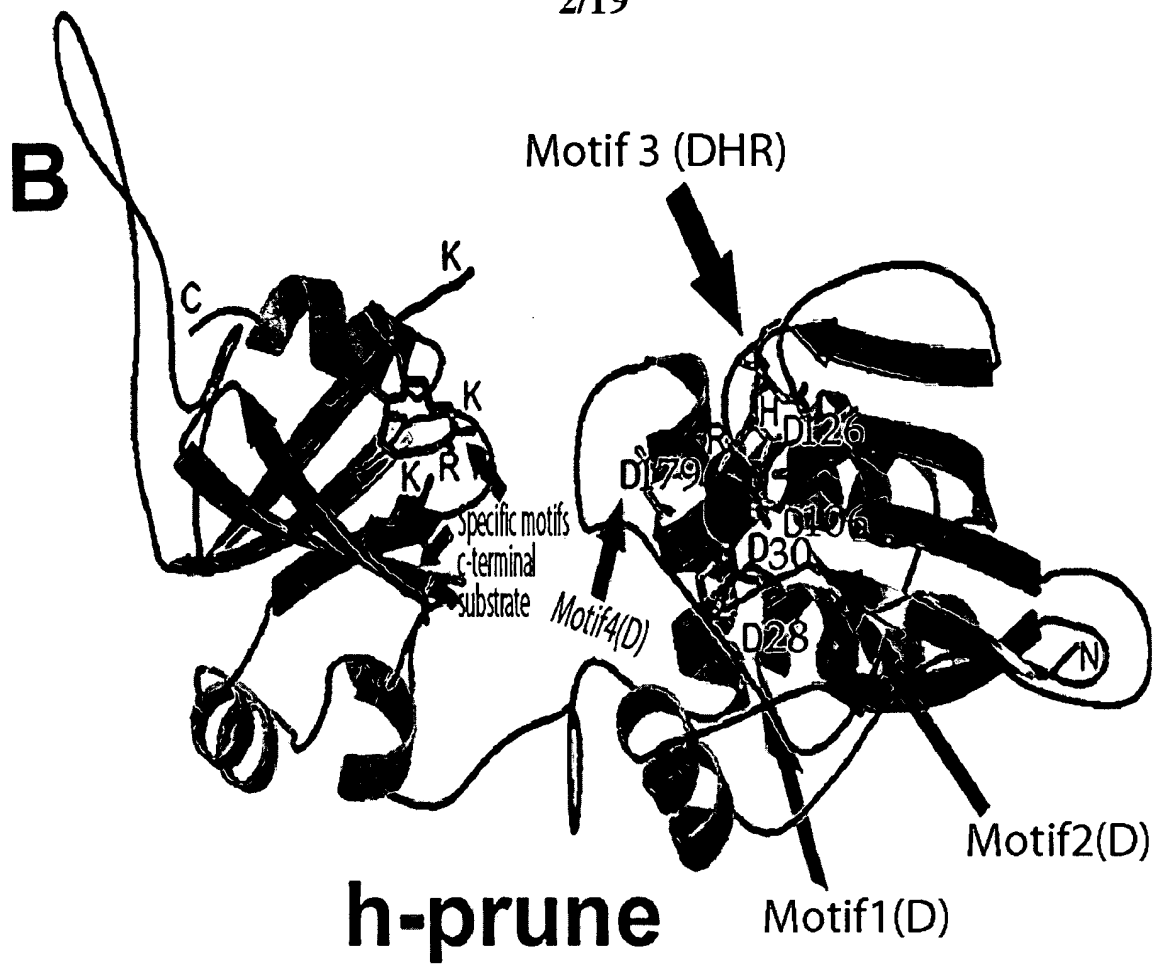
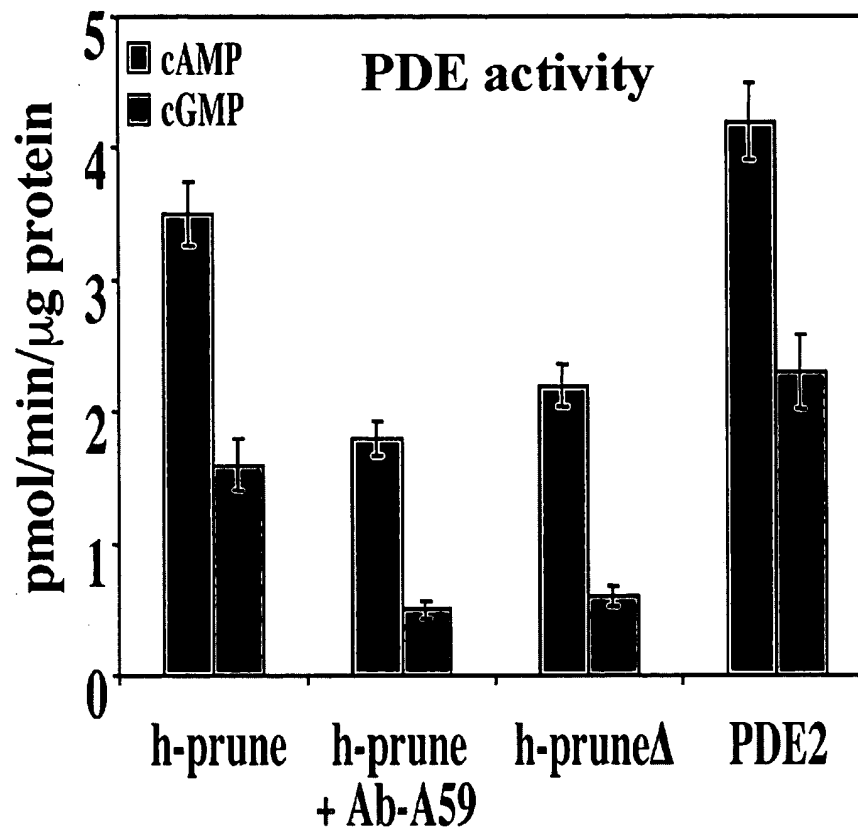
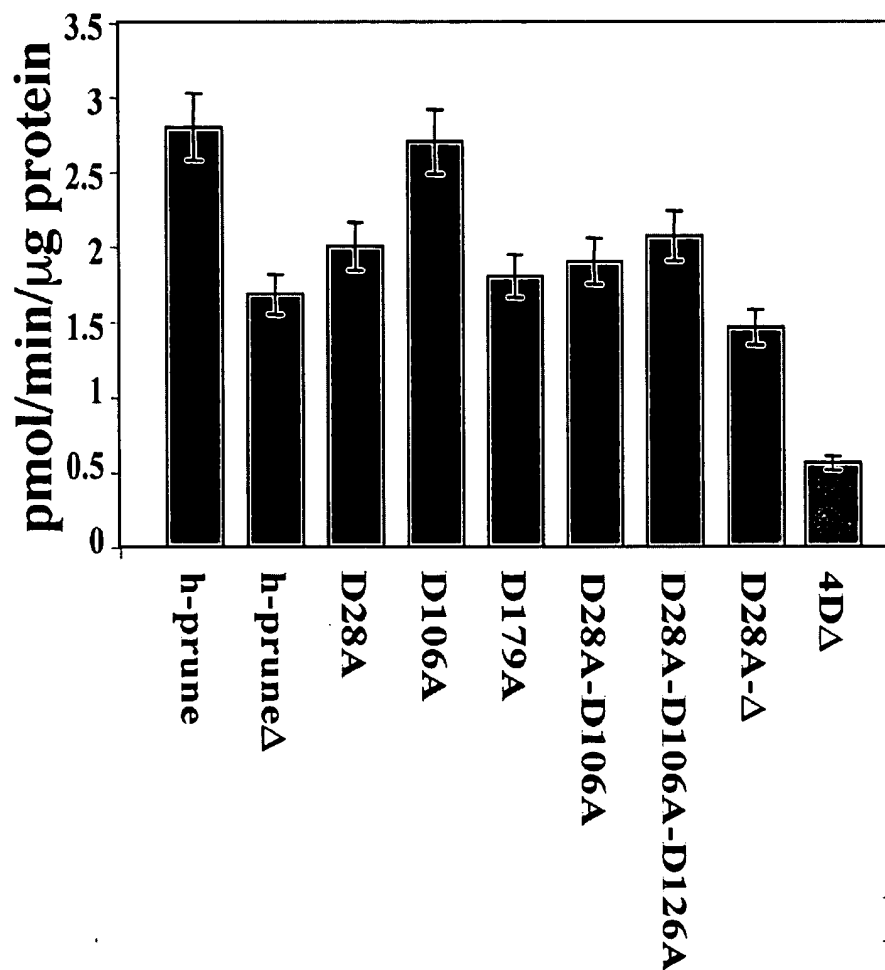
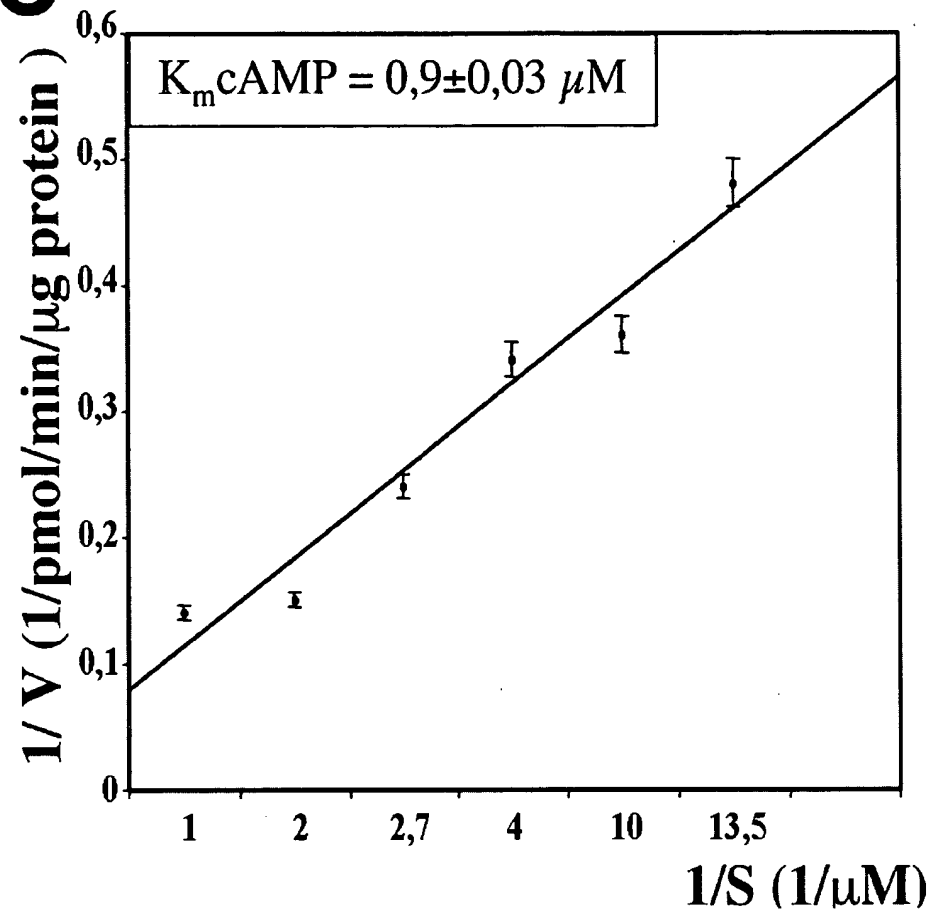
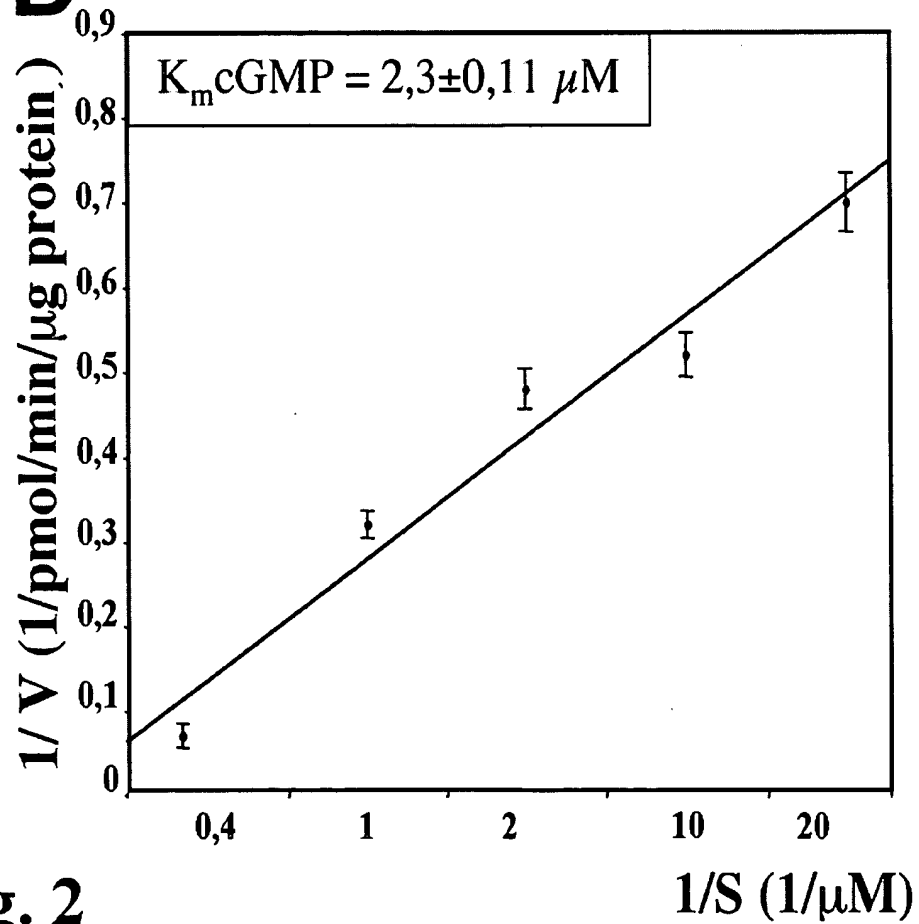
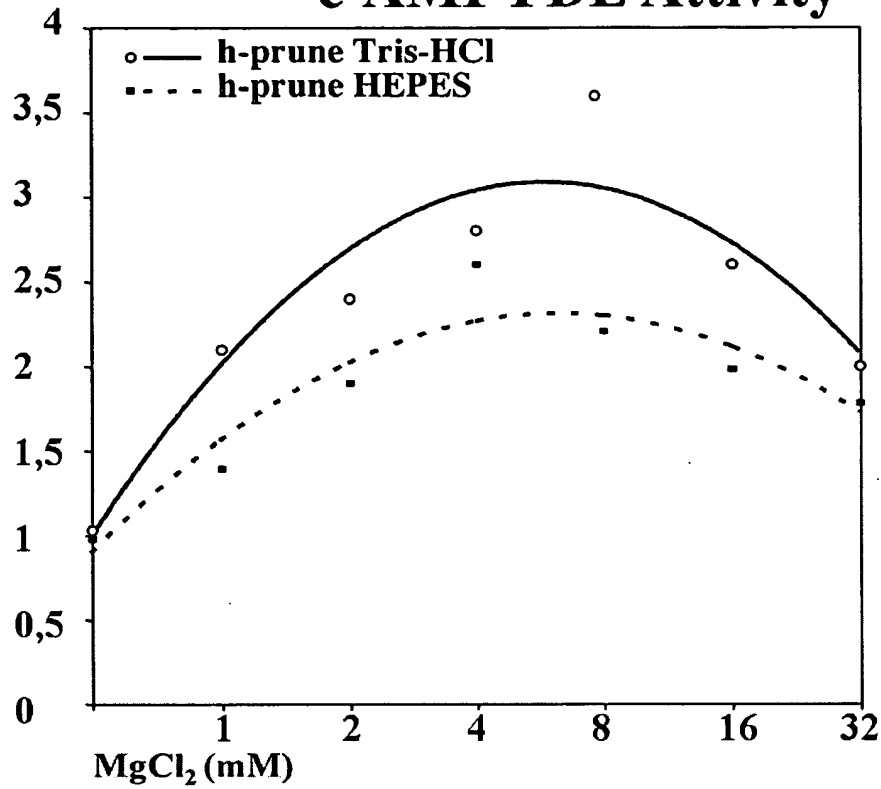
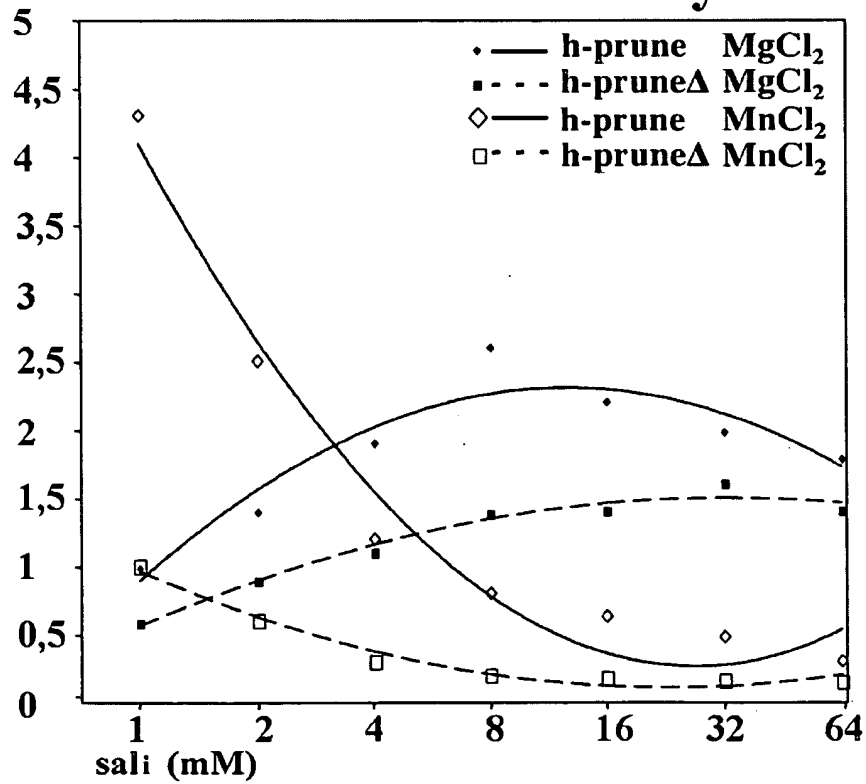
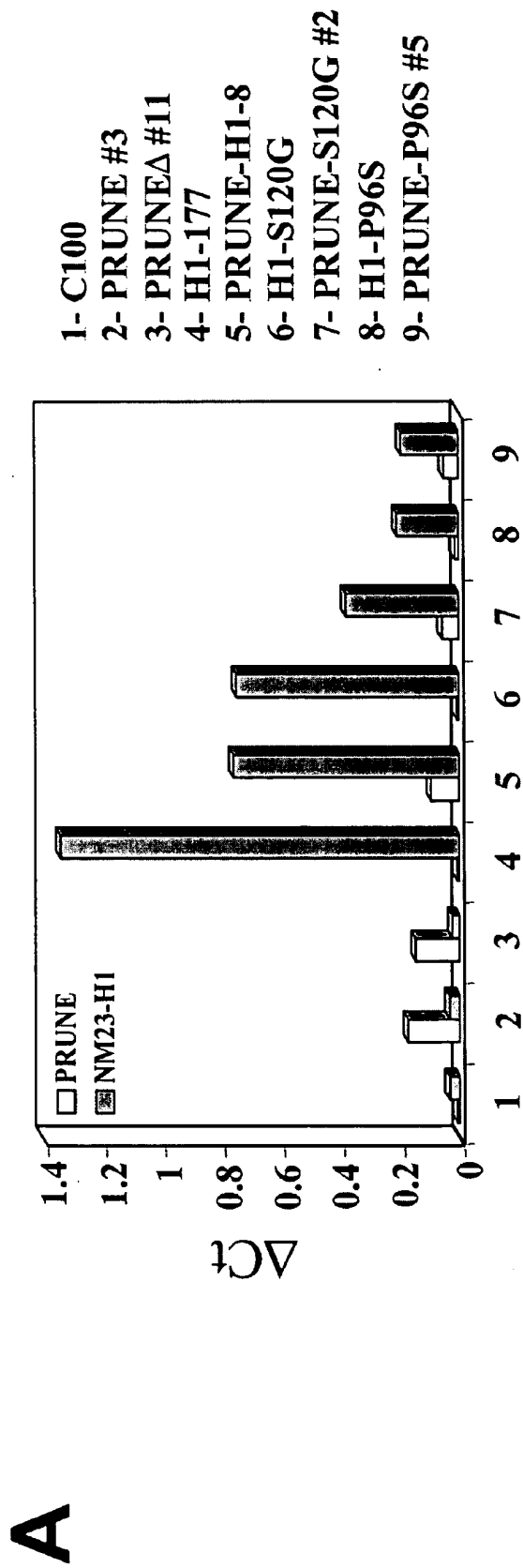
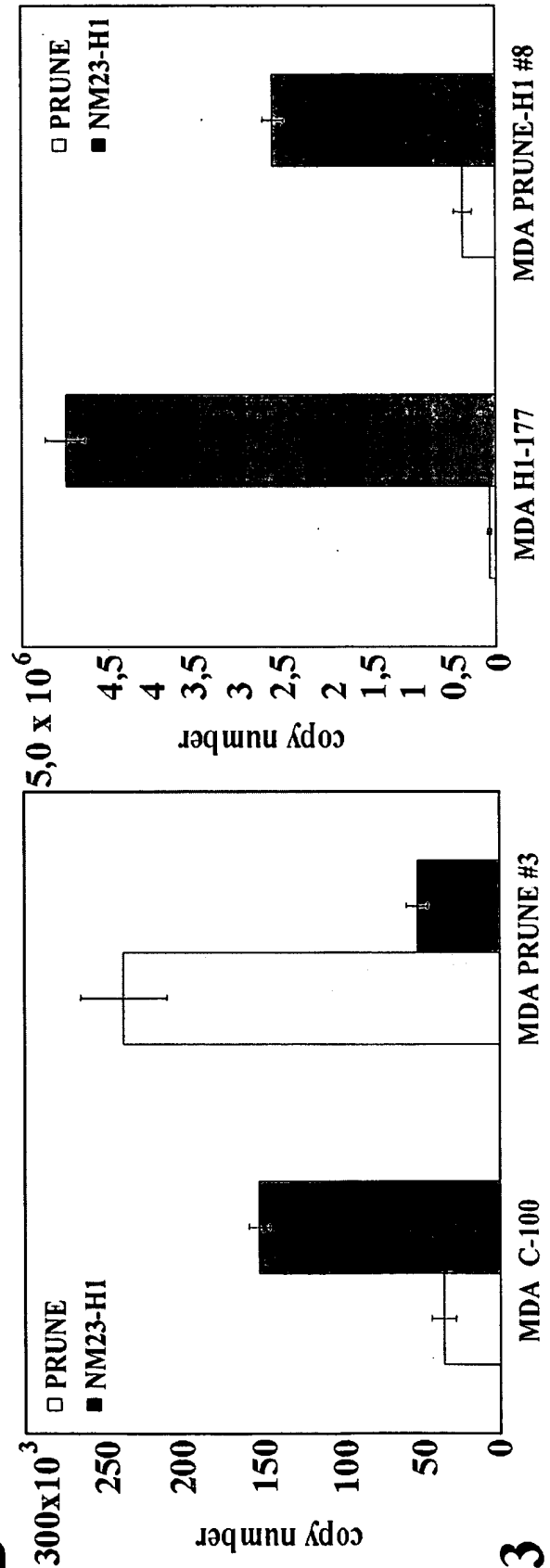


Fig. 1

A**B****Fig. 2**

C**D****Fig. 2**

E**c-AMP PDE Activity****F****c-AMP PDE Activity****Fig. 2**

**B****Fig. 3**

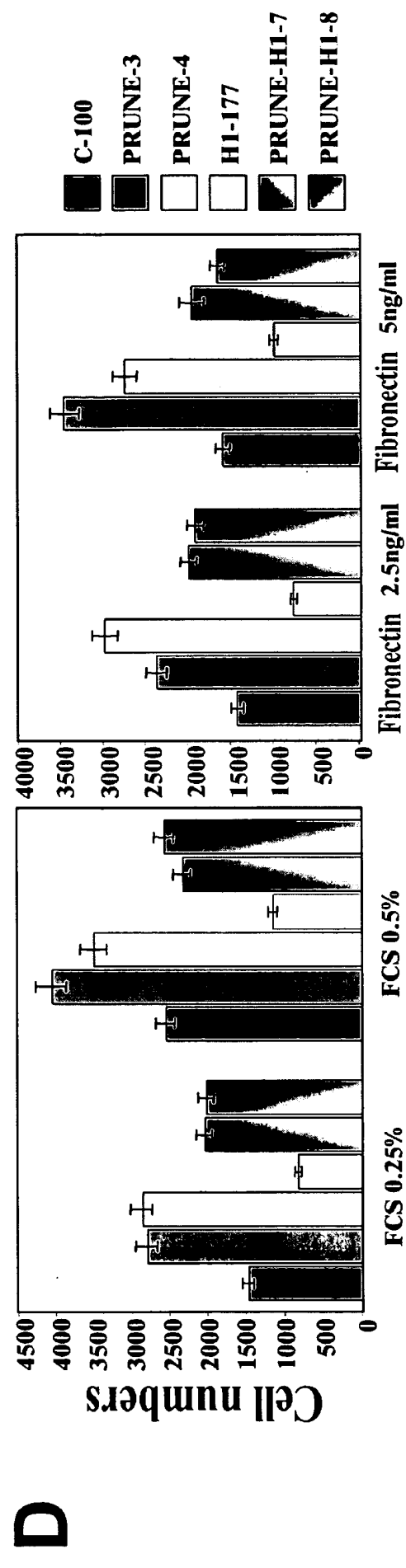
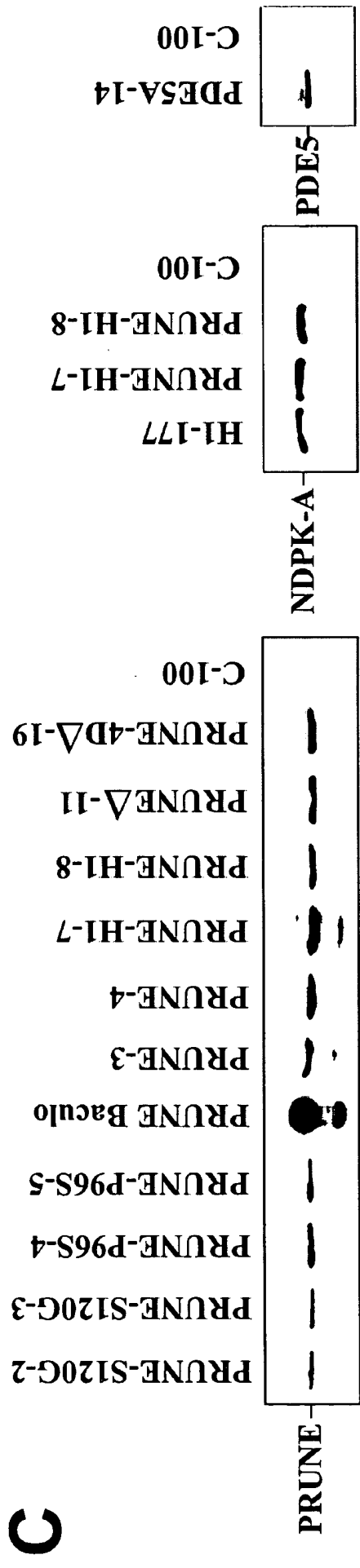
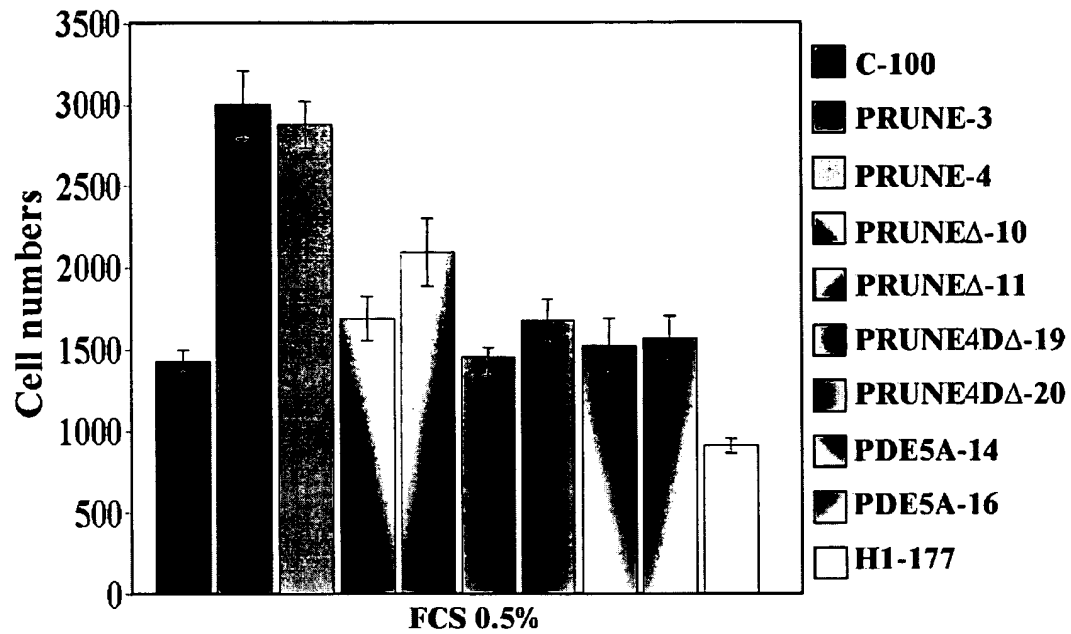
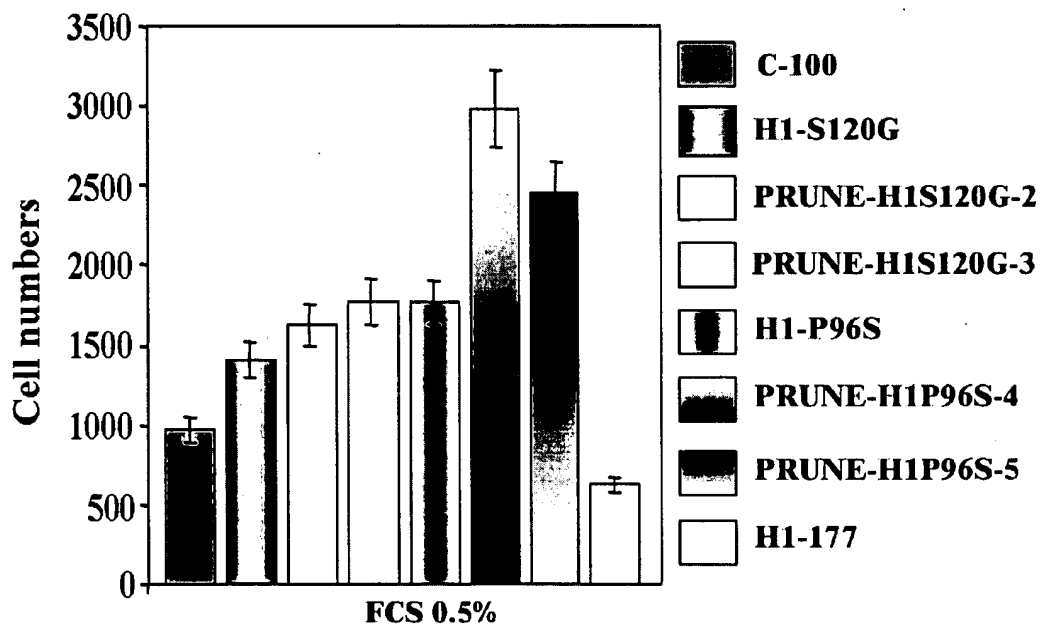
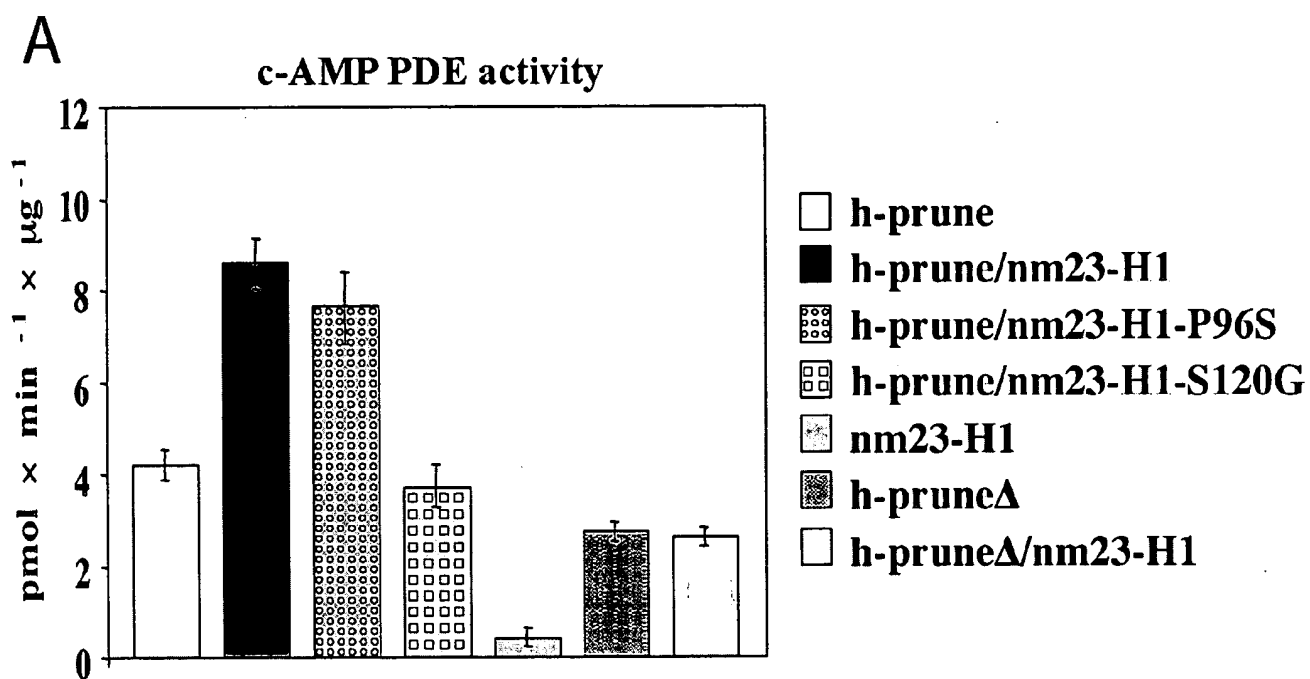


Fig. 3

E**F****Fig. 3**



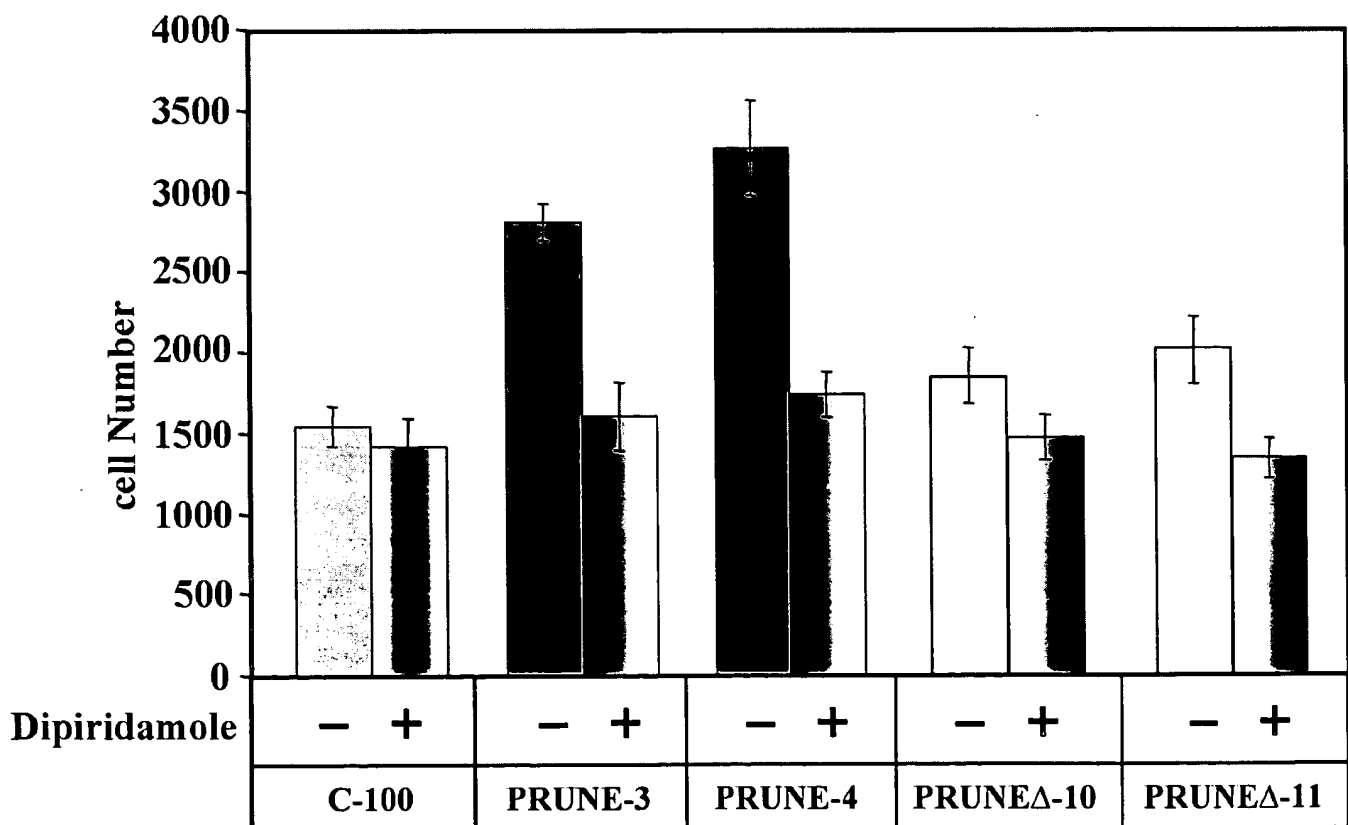
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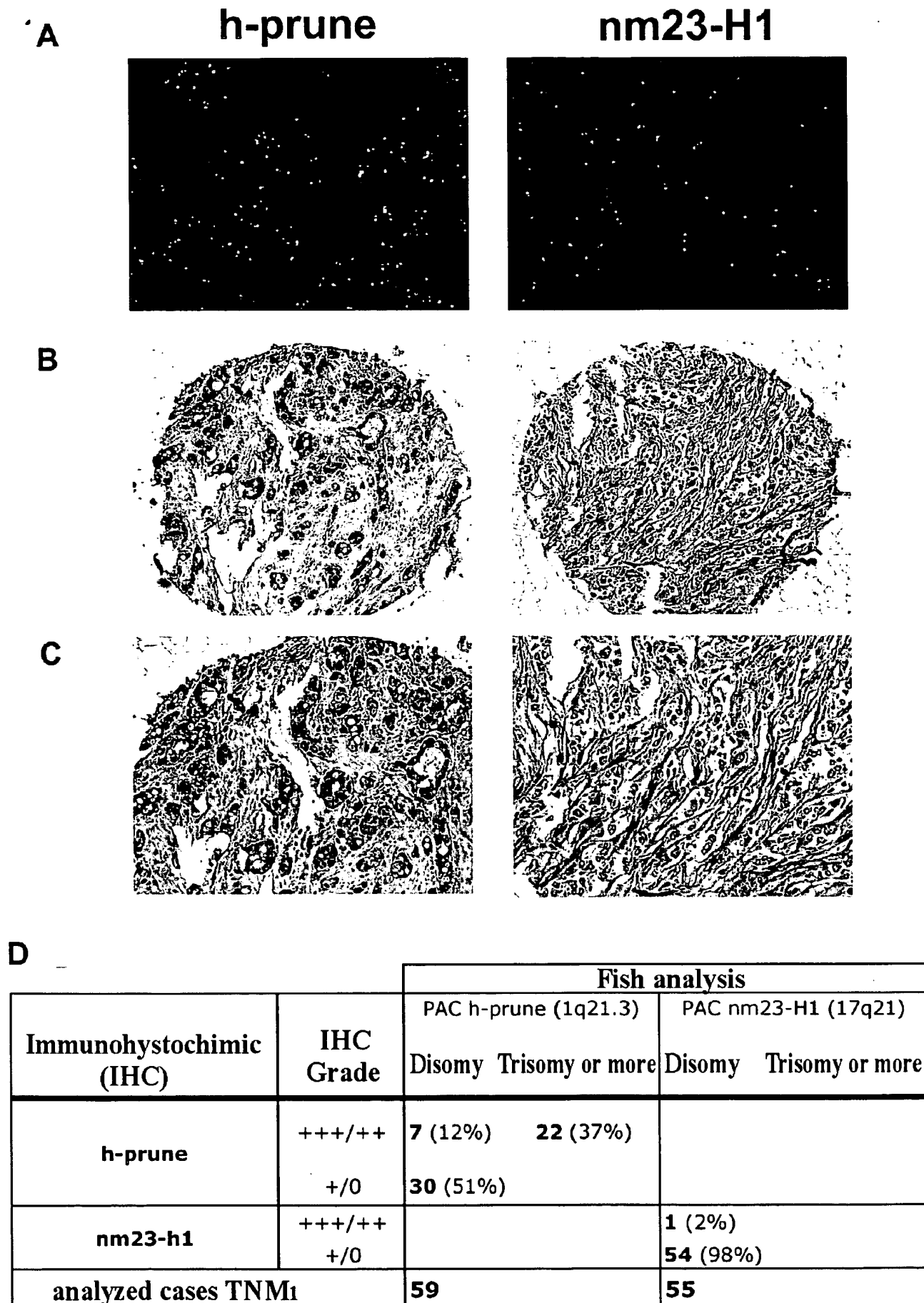
clone name	PDE h-prune Activity (pmol \times min ⁻¹ \times μ g ⁻¹)	Mobility cell number
MDA C-100	3.8 \pm 0.7	1548 \pm 84
MDA H1-177	2.2 \pm 0.4	928 \pm 73
MDA PRUNE #3	35 \pm 5.3	2812 \pm 294
MDA PRUNE #4	28.7 \pm 2.5	3272 \pm 271
MDA PRUNE Δ #10	16.8 \pm 1.2	1682 \pm 64
MDA PRUNE Δ #11	14.6 \pm 0.9	2087 \pm 97
MDA PRUNE-H1 #7	18.8 \pm 2.6	2048 \pm 93
MDA PRUNE-H1 #8	22 \pm 4.2	2006 \pm 87
MDA H1S120G	2.4 \pm 0.8	1328 \pm 54
MDA PRUNE-H1S120G #2	4.4 \pm 1.6	1624 \pm 89
MDA PRUNE-H1S120G #3	5.3 \pm 1.4	1767 \pm 108
MDA H1P96S	3.0 \pm 0.3	1742 \pm 38
MDA PRUNE-H1P96S #4	19.2 \pm 0.3	2982 \pm 184
MDA PRUNE-H1P96S #5	11.6 \pm 0.4	2448 \pm 143

Fig. 4

A

Inibitor	Selective for a PDE type	IC ₅₀ μM	h-prune IC ₅₀ μM
Cilostamide	PDE3	0.05	>100
Dipyridamole	PDE5/6/9/10/11	0.9/0.38/4.5/1.1/0.37	0.78±0.05
IBMX	not selective	2-59	40.2±0.8
Milrinone	PDE3	1.3	>100
Rolipram	PDE4	2.0	>100
Vinpocetine	PDE1C	8.1	22.3±1.1
Zaprinast	PDE1/5/6	6.9/0.76/0.15	>100
Sulindac	cGMP PDEs	—	>100

B**Fig. 5**

**Fig. 6**

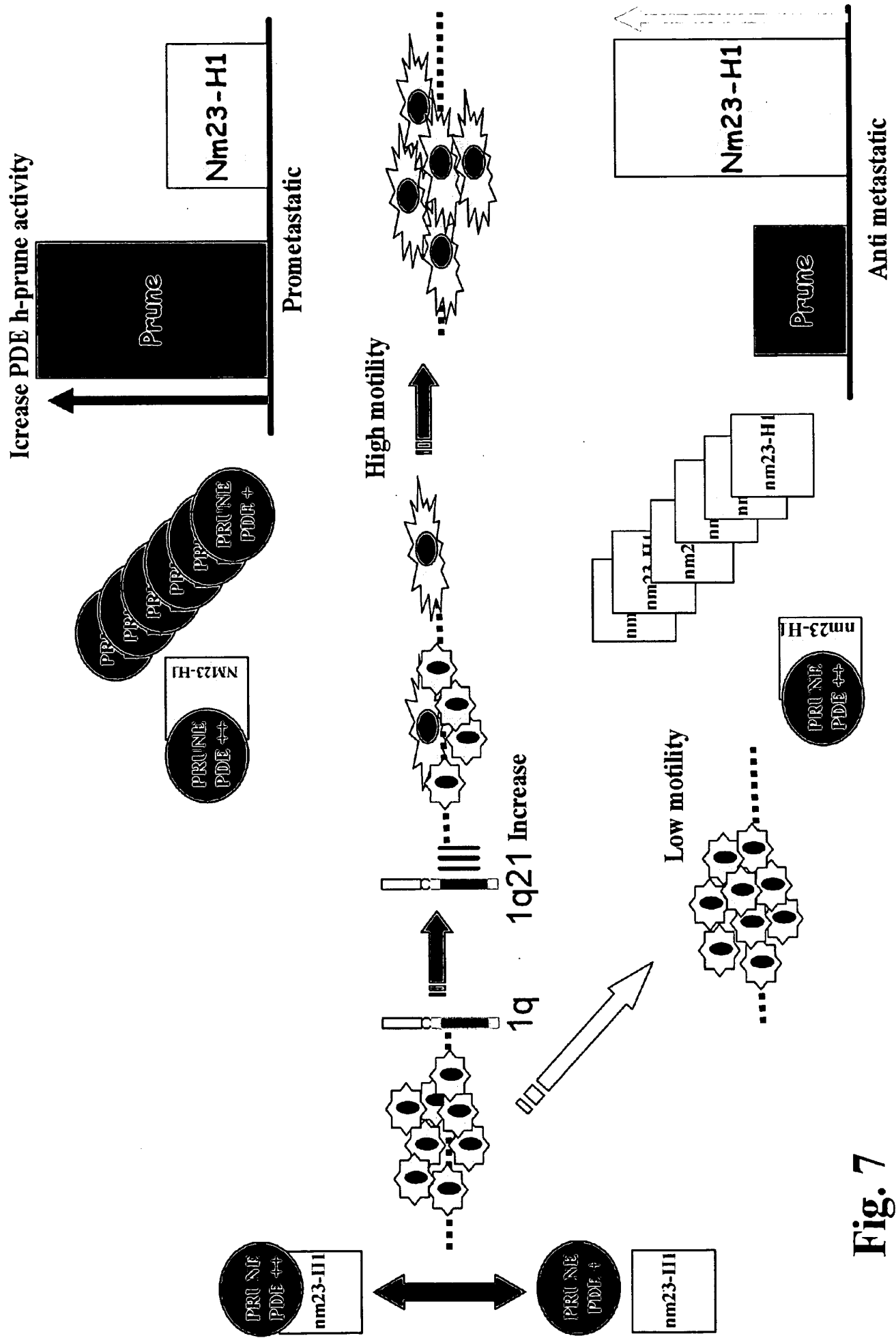
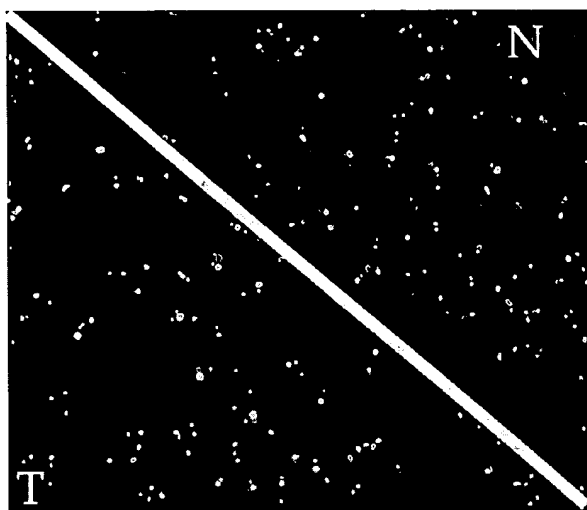
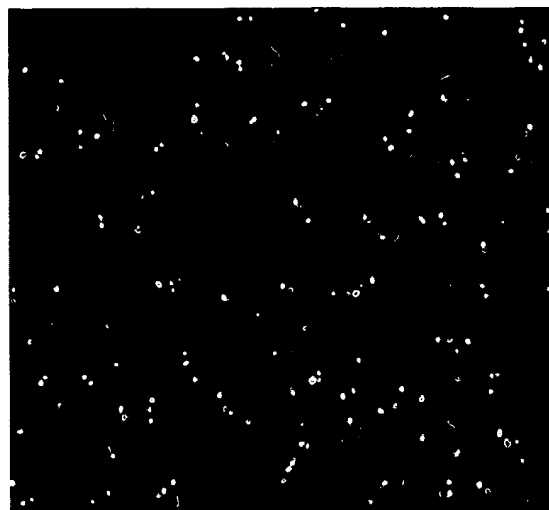


Fig. 7

A

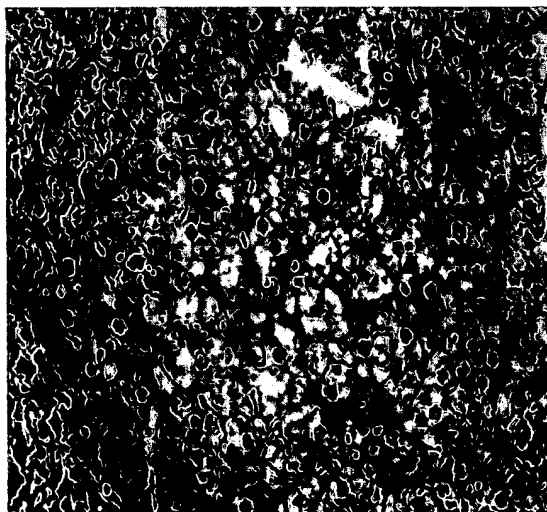


Normal and tumoral tissue



Tumoral tissue
(not metastatic)

B

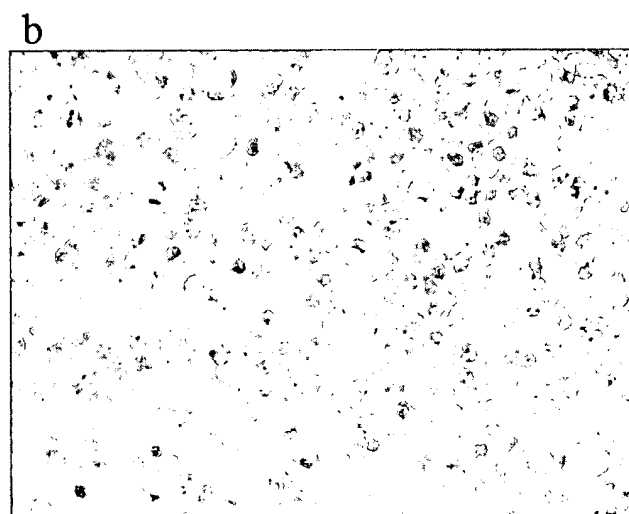
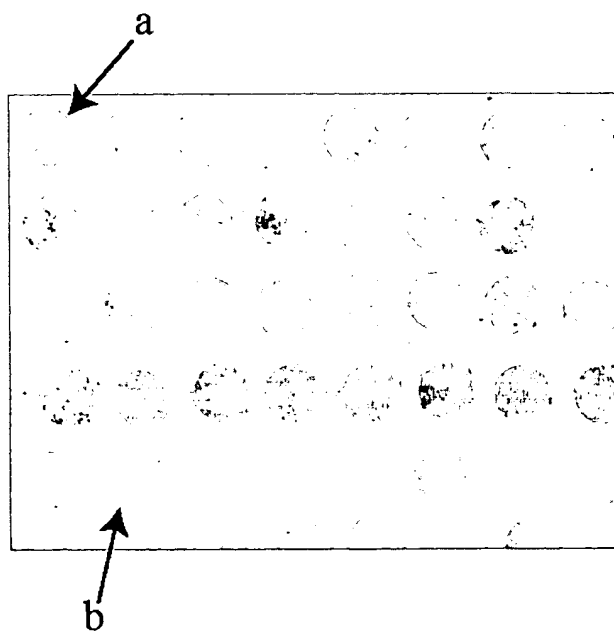


Normal tissue

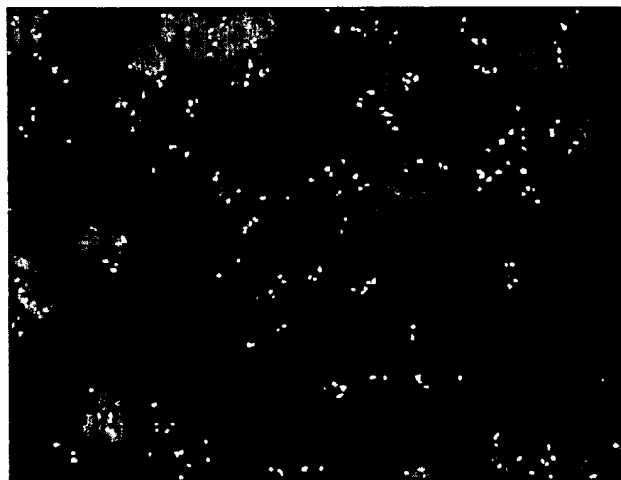


Tumoral tissue
(not metastatic)

Fig. 8



A)

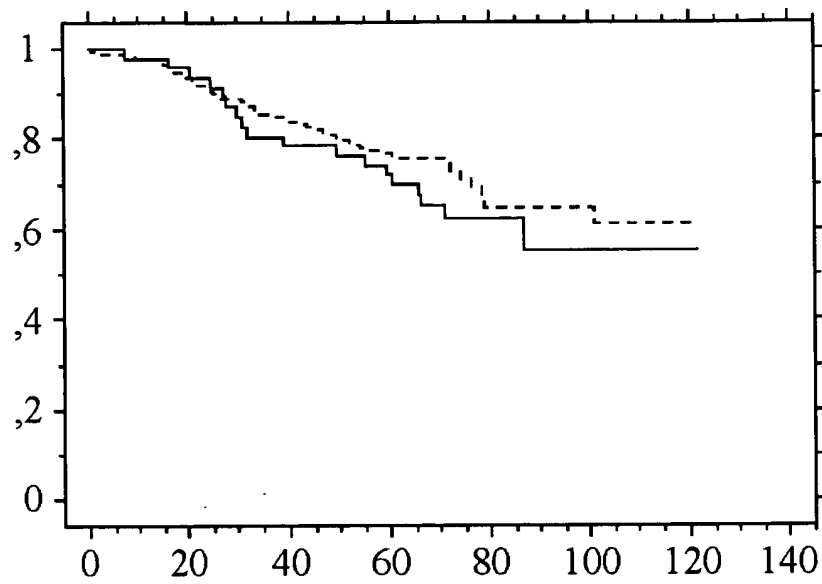


B)

Fig. 9

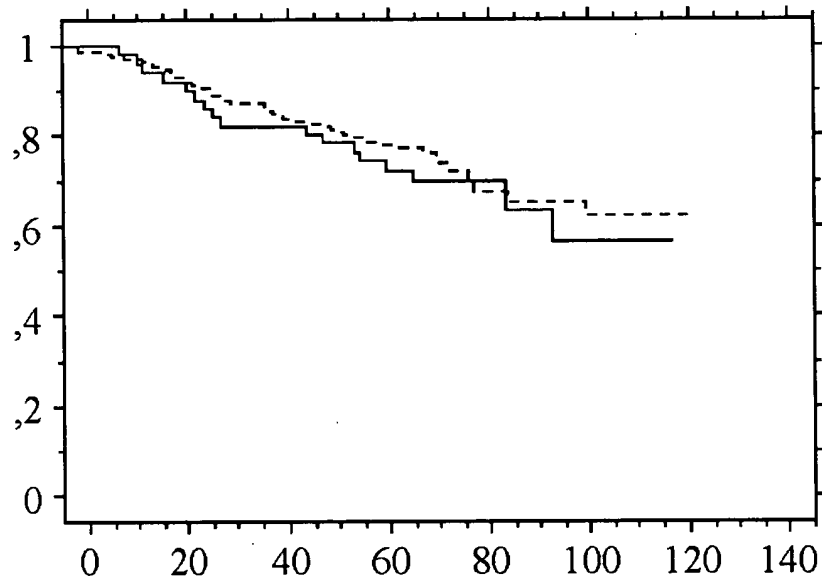
A)

15/19



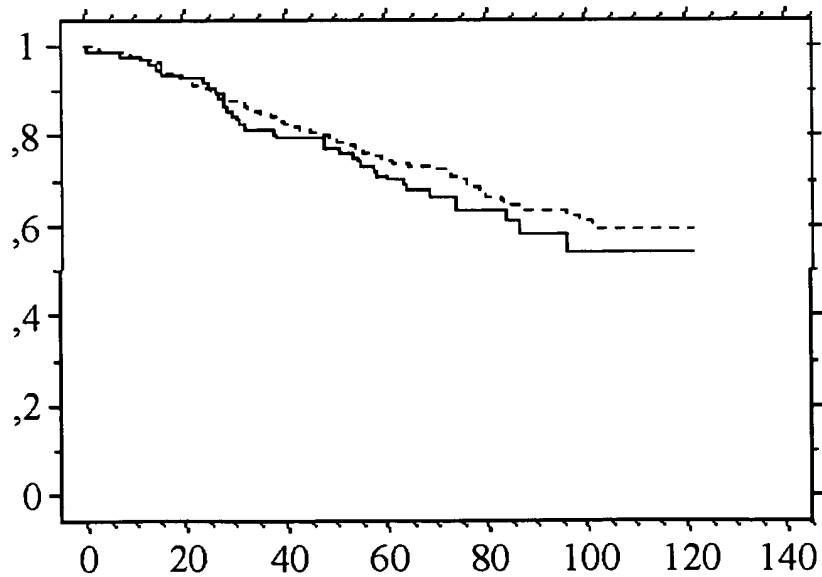
----- nm23-H1 positive
—— nm23-H1 negative

B)



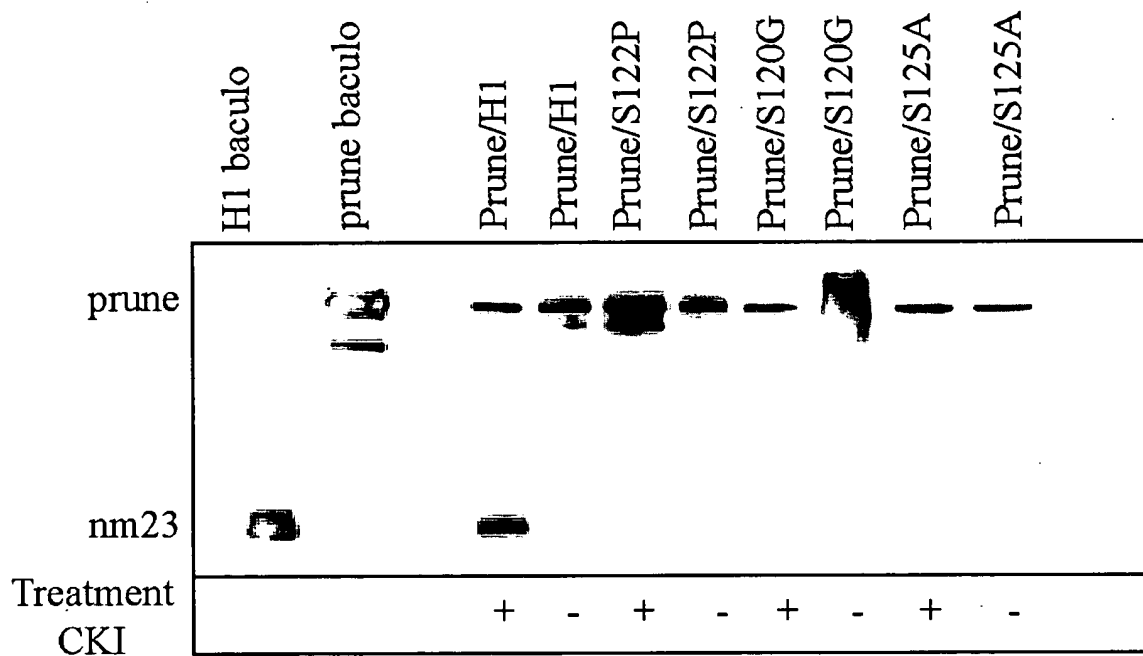
----- h-prune negative
—— h-prune positive

C)



----- h-prune negative
—— h-prune positive

Fig. 10



A)

MYDVPDYASLGSPVEMA
 NLERTFIAIKPDGVQRGLV
 GEIIKRFEQKGFRLVAMK
 FLRASEEHLKQHYIDLKD
 RPFFPGLVKYMNSGPVVA
 MVWEGLNVVKTGRVML
 GETNPADSKPGTIRGDFCI
 QVGRNIIHGSDSVKSAEK
 EISLWFKPEELVDYKSCA
 HDWVYE

B)

Fig. 11

Voyager Spec #1 MC[BP = 1344,6 21449]

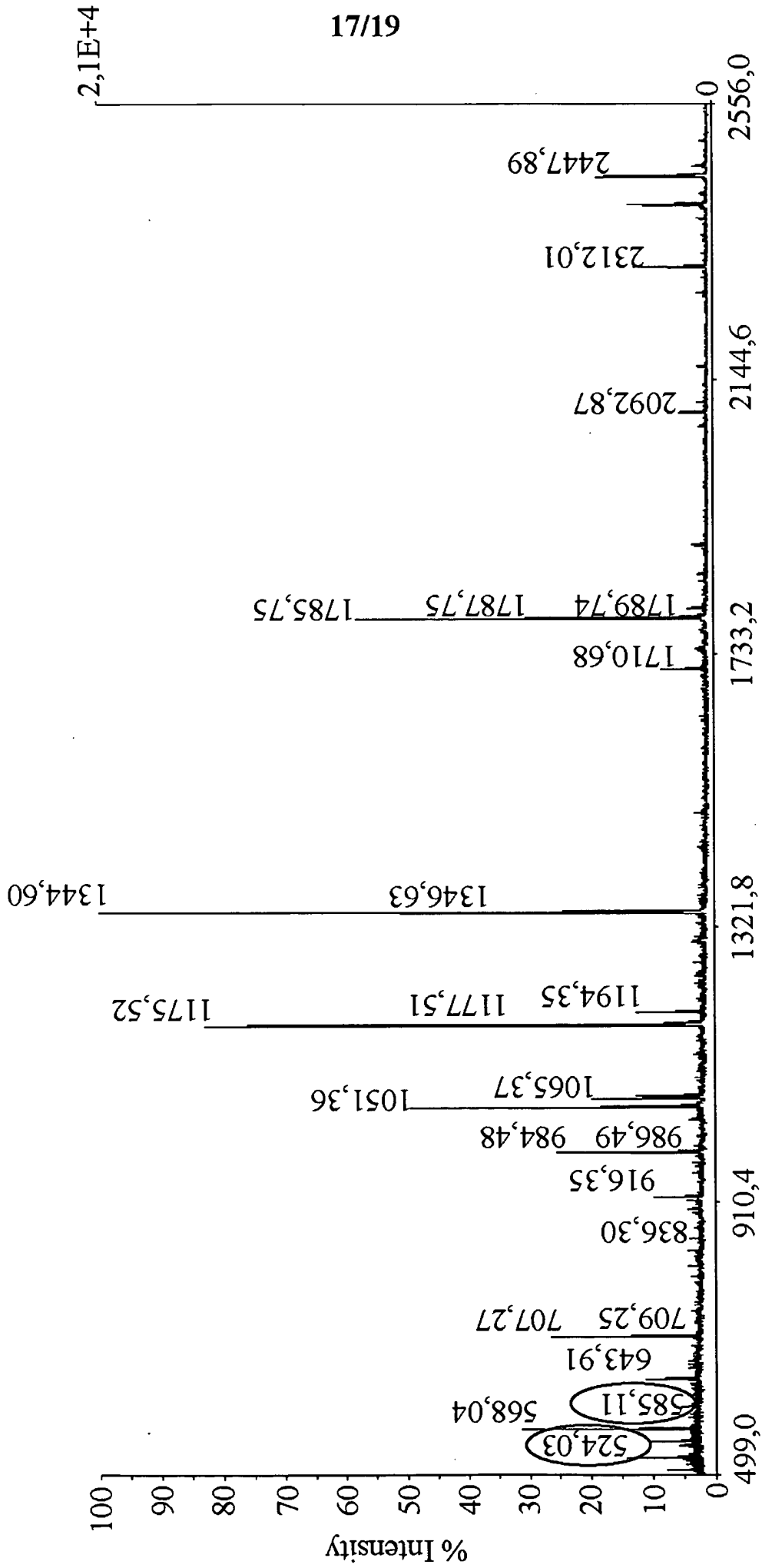


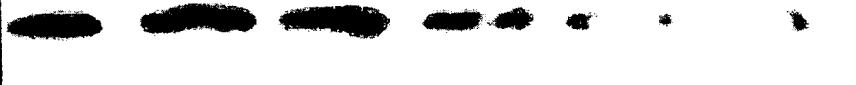
Fig. 11 C

A

	1	2	3	4
CKI8	+	+	-	-
Isoform Nm23	H1	H2	H1	H2

nm23 → 

B

IC261	0h	2h	4h	6h	8h	0h
CIP	—	—	—	—	—	+
Phosphorecated nmZH1						
Total nm23H1						

C

	1	2	3	4	5
IC261 μ Mol		50	200	—	

h-prune → 

nm23H1 → 

Fig. 12

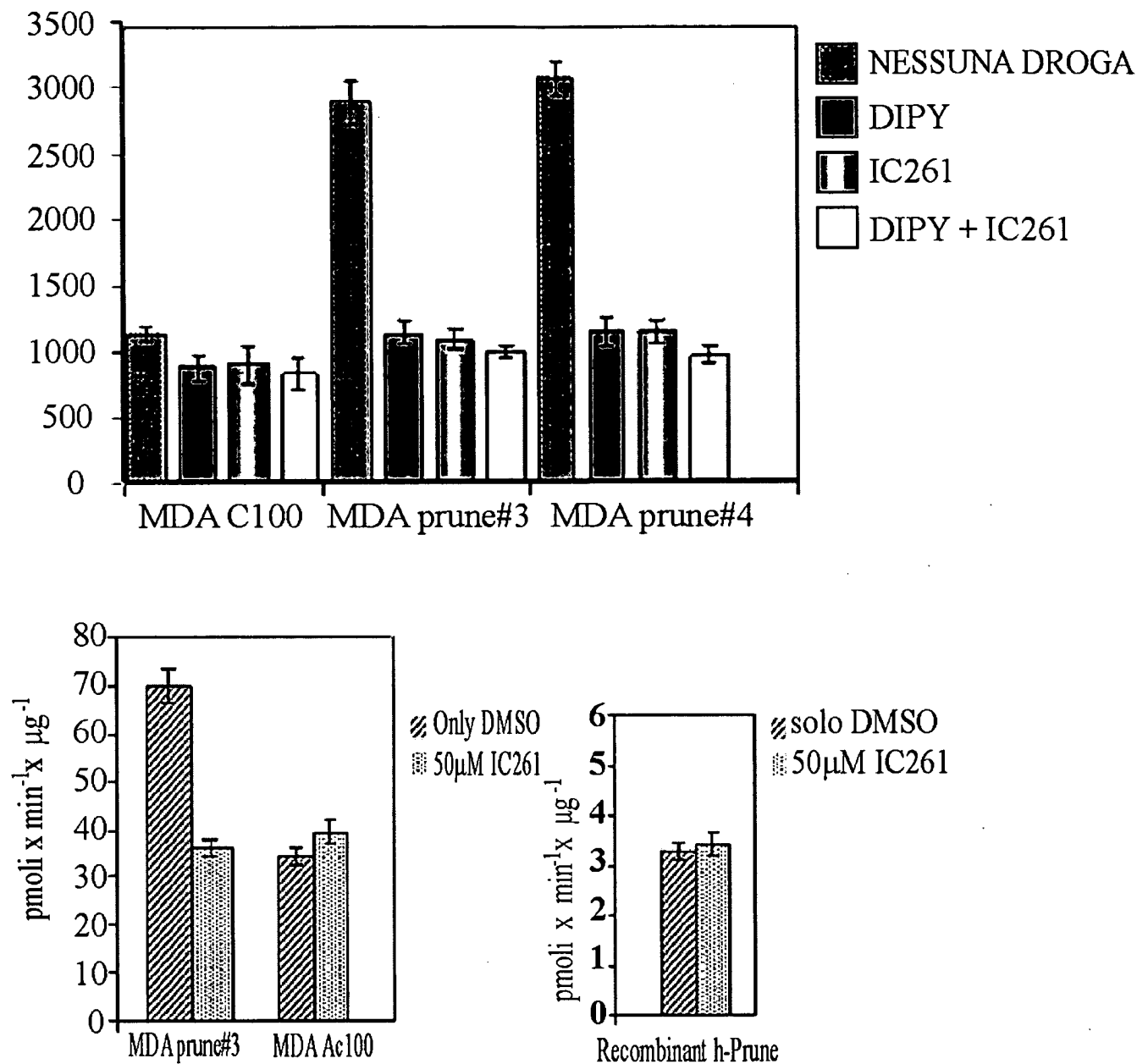


Fig. 13

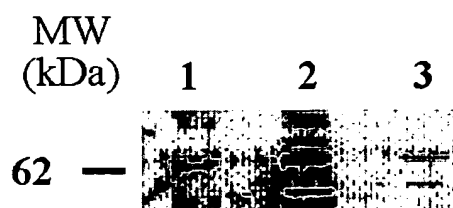


Fig. 14